



The Gustav Stern Symposium

# Perspectives in Virology

*Volume 10*

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## Preface

*Perspectives in Virology*, Volume 10 illustrates the diverse and dynamic nature of virology. This volume covers new developments in basic and in applied virology which expand the horizons and improve comprehension. It reports the first confirmed *in vitro* propagation of hepatitis B antigen, the genetic analysis of virulence in influenza viruses, an assessment of viral insecticides, new human virus diseases, the viruses of human warts, and other subjects. This volume honors the important contributions of Werner and Gertrude Henle to the field of virology. It demonstrates the continued commitment to virology of the Gustav Stern Foundation, personified by Irene Stern. I thank her for constant interest in and support for this important area of science. I express my sincere thanks to members of the program committee, and to all who identify with virology for their help and interest in the development of this publication.

Morris Pollard  
Notre Dame, Indiana

## Editor's Foreword

Twenty years ago, after the death of virologist F. R. Beaudette of Rutgers University, Mr. and Mrs. Gustav Stern invited a group of scientists to their home, to recommend a way by which the talents and contributions of their friend and science advisor could be recognized and appreciated. Gathered there were J. W. Beard, Rene Dubos, Robert Huebner, R. E. Shope, James H. Steele, and myself. From this conference came the First Symposium on Perspectives in Virology, which was held in 1958 at the Park Sheraton Hotel in New York. A significant number of participants in the first symposium, 21 years ago, are here at the Tenth Symposium.

We miss, with affection, many of the remembered stalwart friends and contributors to virology (including Gustav Stern). Their leadership roles in science are being, and will be, taken by many of the younger people here this evening. I personally miss the driving dynamic personality of Gustav Stern, who was a tough, demanding teacher. His purpose in these symposia was that society be the beneficiary of our efforts. Irene Stern promotes these ideals with the same determination, even to the extent of sponsoring additional conferences on exotic diseases.

This volume is based on the Tenth Gustav Stern Symposium on *Perspectives in Virology*. A commitment was made 18 years ago by the Stern family that they and their resources would support and promote the field of virology; and their fulfilled pledge has resulted in memorable and fruitful experiences for all of us. What was initiated as a gesture of affection for F. R. Beaudette, has become a unique, internationally recognized forum for recognition of virologists, of their new horizons and developments. We gratefully recognize the contributions to biomedical science of the sponsor, Mrs. Irene Stern, and the Foundation that she heads. I wish to convey from all of us to her and her family, our appreciation for their positive contributions to the social orders which we all serve.

Morris Pollard



Werner and Gertrude Henle

## Foreword: In Honor of Werner and Gertrude Henle

The Tenth Gustav Stern Symposium on *Perspectives in Virology* honors two outstanding virologists who contributed in great measure to the explosive growth and development of virology, a development experienced by few areas of science. The Drs. Werner and Gertrude Henle (Werner and Brigitte, as they are known to most of us here) join the gallery of those honored by previous Gustav Stern Symposia: Dr. Fred Baudette, 1958; Dr. Peyton Rous, 1960; Dr. Richard E. Shope, 1962; Dr. Wendell M. Stanley, 1964; Dr. John F. Enders, 1968; Mr. Gustav Stern, 1970; Dr. Thomas H. Weller, 1972; and Sir Christopher H. Andrewes, 1974. \*

Many of us regard the Stern Symposia as ideal scientific gatherings: each symposium focused on a specific theme, and each provides opportunities for exchange of ideas between established senior scientists and the young, restlessly probing and questioning researchers in a setting which has fostered fruitful scientific debate.

The contributions of the Drs. Henle to science and in particular to virology are so many that it would be difficult to decide which of their many accomplishments is the most outstanding. Both were born a few years before the first World War in Germany, both graduated from the University of Heidelberg and served their internships at the University of Heidelberg and the Kaiser-Wilhelm Institute (now the Max Planck Institute) in Heidelberg before joining the research department of the Children's Hospital of Philadelphia under the directorship of Joseph Stokes, Jr., in 1936 and 1937 respectively. It is characteristic of the Drs. Henle that they stayed at that institution for their entire scientific careers, working diligently and quietly, not striving for more pretentious positions but devoting their time, energies and sometimes impatience to the pursuit of their studies.

From Werner Henle's first publication on "Die serologische Sonderstellung des Speichels" with Ernest Witebsky in the *Zeitschrift fuer Immunitaetsforschung* in the politically fateful year of 1933 and the first publication in 1936 with Gertrude Szpingier (who soon thereafter became Gertrude Henle) to today, more than 300 publications later, both Werner and Gertrude Henle advanced virology to an immeasurable extent. They had already published a series of classical but often forgotten papers on studies of immunological fertility control before Werner was transformed instantly into a virologist by a one-day visit to Dr. Parker's laboratory in 1940 to learn tissue culture. As Werner himself tells us, he was sent by Dr. Stokes for an indefinite time to the research department of Squibb at Princeton. On arrival in Dr. Parker's laboratory he was told that a transfer of a tissue culture, the original permanent chick heart culture of Carrel, was about to take place and that he was permitted to observe. Everybody dressed in surgical attire with gloves and

masks: the master transferred the culture from one culture vessel to another, added fresh medium and chick embryo extract containing fresh fibroblasts—thus assuring “the immortality of the heart culture”—and in the manner of great surgeons, walked away. Dr. Henle was then told that he had now seen all there was to see and he could return home to start his own work. The virologist Werner Henle was born. He went home, taught all he had learned to his wife and co-worker, and they began work on influenza virus. They began by using chick embryos rather than cell cultures as culture media for virus replication. The technique of using allantoic membranes of deembryonated eggs as a culture provided naturally with its own culture vessel, the egg shell, was developed in their laboratories, and this early and important development produced the first usable system for accurate, one-step growth curves of influenza virus. The contributions of the Henles to the understanding of influenza virus multiplication, its antigenic composition and variations and the immune response to live and inactivated influenza viruses are numerous and were significant in developing influenza virus vaccines. In the late 1940s they broadened their interest to include studies of paramyxoviruses. The soluble and viral antigens of mumps virus were identified and the antibody responses of persons undergoing a natural infection or of persons vaccinated with killed mumps virus vaccine were evaluated. The minimal height of antibody titers needed for protection against infection with virulent virus, and the optimal doses and schedules for vaccination with inactivated mumps virus vaccines were determined. Studies of the isolation and serial passage of mumps virus in avian and mammalian cell cultures led to the recognition and exact measurement of the degree of attenuation of mumps viruses in avian cells which allowed later the commercial development of a live attenuated mumps virus vaccine.

Attempts to transmit human hepatitis viruses to chick embryos in the 1950s were not entirely successful, although some of these experiments should be repeated today using genetically controlled leucosis-free chick embryos and modern techniques for the detection of hepatitis virus antigens before dismissing these studies as negative.

The Henles' studies of persistent infection of cell cultures with Newcastle disease (NDV) and mumps viruses were among the first to probe the host cell-virus interrelationships governing the simultaneous survival both of viruses and cells, maintaining virus and cell replication in a delicate balance. The role of interferon in these systems was elucidated and these as well as similar experimental models were used later by many laboratories for detailed studies on the cellular or cell population level. These investigations, done before the importance of viral persistence in the pathogenesis of a number of diseases was recognized, attest to the foresight which the Drs. Henle have demonstrated throughout their career.

Entrance into the field of tumor virology came with studies by Gertrude Henle on polyoma virus in 1958/59 and these were followed by the now classical studies on the association of Epstein Barr virus (EBV) with



Burkitt's lymphoma and nasopharyngeal carcinoma and the proof that EBV causes infectious mononucleosis.

These achievements alone would justify the honor and respect in which Werner and Gertrude Henle are held and their recognition tonight but above and beyond their own achievements they have given most generously of their time to others. Both have been members of numerous national and international advisory groups; most recently Werner was a member of the National Cancer Advisory Board and they have both influenced development of virus-cancer research here and abroad. But perhaps most important has been and continues to be their influence on the further development of virology by the large number of scientists who have passed through their laboratories, staying for shorter or longer periods of time. Little did I think myself when I was sitting in the very lecture hall in Goettingen, in which Werner Henle's grandfather, Jacob Henle, the discoverer of Henle's loop of the kidney, had taught anatomy years ago, that my professional career would be determined by seven years training in the laboratories of the grandson of this distinguished anatomist of the 19th century. The doors of the Henle laboratories in Philadelphia were always wide open for those who wanted to learn and their house in Bala Cynwyd for continuation of scientific discussion or for help with whatever problems arose. There was challenge, hard work, understanding and concern for so many students and fellows from all over the world who made their intellectual home for some time in the virology laboratories of Children's Hospital. Many of them today are heads of departments or laboratories and the generation of intellectual grandchildren is rapidly growing with the first great grandchildren just stepping out of the wings. I speak for all the previous trainees of Werner and Gertrude Henle when I thank them for their guidance of our first steps in the world of experimental biological research.

Recognitions of the Henle's accomplishments have been given during recent years; to name only a few, Werner Henle was elected to the National Academy of Sciences, he was awarded an honorary Doctor's degree from the University of Basel and Gertrude Henle from the University of Philadelphia. They received jointly the Robert Koch Award, the Robert de Villiers Award in Cancer Immunology, Cancer Research Institute Inc. New York and the Virus Cancer Program Award, National Cancer Institute.

Werner and Gertrude Henle contributed so much to the basic understanding of virus-host cell interrelationships but they did not isolate themselves in an ivory laboratory. They never lost sight of the role their findings played in the pathogenesis of disease, and they continue to show us how questions posed in biological terms, even in the age of molecular biology, continue to be crucial to advancing our understanding of viral disease.

For all your contributions we are grateful to you both. We wish you many more years of active and happy scientific and private life, and many more contributions to the advancement of our science.

Friedrich Deinhardt, M.D.

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